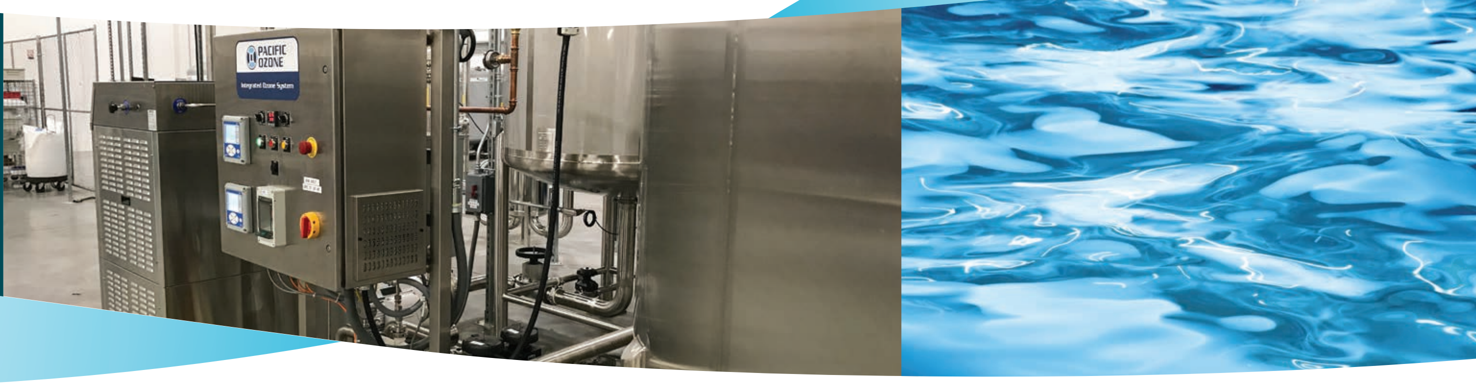
PACIFIC OZONE™ an evoqua brand | ADVANCED DISINFECTION

APPLICATION NOTE



COMMISSIONING & QUALIFICATION FOR PHARMACEUTICAL WATER SYSTEMS

DISINFECTION OF PURE WATER SYSTEMS

Packaged systems offer greater reliability and efficacy, use best practices to eliminate variables common in on-site integrated ozone systems used in pharmaceutical, biotech and personal care. The approach is innovative, providing known results with new tools that quantify steady-state dissolved ozone levels and mass transfer efficiency, decrease the risk of misapplication, and increase success.

Users of industrial pure water systems pursue lower maintenance and operational costs, increased reliability, and improved life cycle management. Innovative methods and newer technology exist to increase throughput, quality, and uptime. Ozone solutions are an advanced disinfection technology that delivers the most powerful commercially available oxidant and disinfectant with few detrimental issues. Ozone sanitization and disinfection has been used for decades, and its adoption in biopharm and personal care water systems has been increasing for several years.

When used in lieu of hot water or chemical sanitization for ambient-temperature purified-water systems, ozone prevents the accumulation of microbials and organics and requires less maintenance over the life cycle of the water system.

Advantages of Ozone Disinfection at 24/7 Administration

- 85% less expensive than hot water sanitization five times a week
- 20% less expensive than once-weekly hot water sanitization
- Tens of thousands of dollars less than twice yearly chemical sanitization [1, 2]

Benefits of Complete Packaged Ozone Systems
Supports Commissioning & Qualification
Established Performance Characteristics
Integrates Tightly with UV Destruct
Offers Superior Reliability
Uses Science Based Approach
Includes Analyzers & Instruments
Delivers State-of-the-Art Tank Mixing Technology
Reduces Process Variables
Highest Level of Safety

SIMPLE. PROVEN. OZONE TECHNOLOGY.

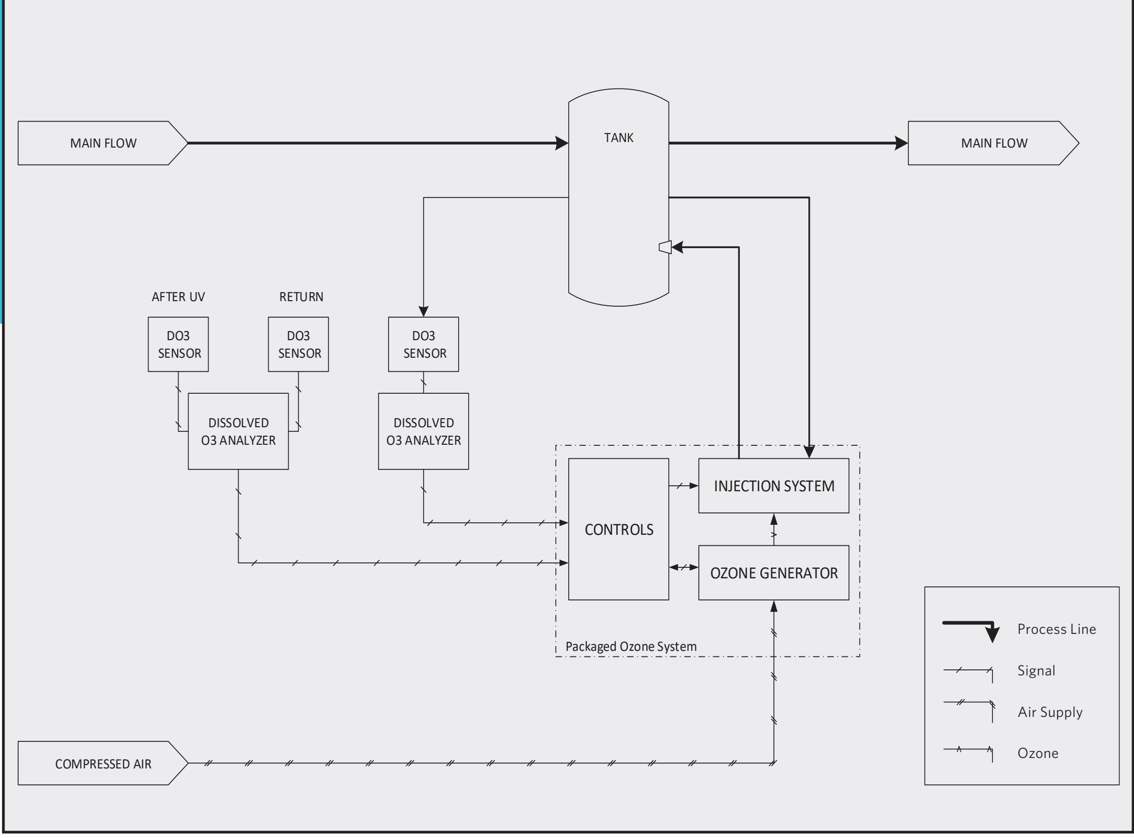


Figure 1: Packaged ozone system process flow diagram.

THE BACKGROUND OF OZONE

Ozone (O3) is triatomic oxygen, which oxidizes carbon compounds in water to carbon dioxide (CO2) when sufficient ozone and time are provided. Since microbials, bacteria, pathogens, and endotoxins all contain carbon, ozone is an excellent biocide that destroys these organisms by oxidation.

There are three ways to produce ozone:

1. Electrolysis
2. UV production
3. Corona discharge

Corona discharge is the most efficient commercialized method for ozone production. It uses a reaction chamber with a dielectric barrier in which high voltage is applied to an oxygen feed gas to generate ozone. Modern corona discharge units are adjustable to throttle ozone production up or down under dynamic conditions when load and demands change. Most advanced corona discharge ozone generators use enriched oxygen from oxygen concentrators (usually +90% by weight) as the feed gas for more efficient ozone production and lower overall operating costs.

The aqueous ozone process consists of four steps:

1. Ozone generation
2. Mass transfer
3. Concentration and contact (residence) time
4. Process control

OZONE EFFICIENCY

Ozone has a short half-life (the time required for the ozone concentration to dissipate to 50%). In 25˚C water, 50% of the ozone decays in approximately 15 minutes (Table A). Different temperatures and water chemistries influence this rate. Ozone reverts to oxygen more rapidly at higher temperatures, for example.

ºC	MINUTES
15	30
20	20
25	15
30	12
35	8

Table A: DO_3 half-life as a function of water temperature (pH 7).

Ozone's short half-life allows disinfection regimes to be calculated easily, according to the concentration required to achieve the desired effect: maintaining pristine systems devoid of microbials and organics. Table B shows a simplified example of these calculations and how to assess the ozone needed for a given concentration.

PACKAGED OZONE SYSTEM COMPONENTS

To configure and control the variables inherent in oxidation processes, packaged ozone systems can minimize the discrepancies associated with individual components and maximize the efficiency and ease of system validation. Components can be tested, integrated, and validated for all performance characteristics by the manufacturer using process analytical technology (PAT), since all measurement, testing, and feedback mechanisms are integrated. This enables monitoring and verification of all instrumentation and process parameters in real time, and offers immediate information on the process and its adherence to the user requirements specifications. The installation/operational qualification (IOQ) phase can easily be integrated; commissioning and qualification can be performed readily with continuous monitoring, using PAT for validation.

Typical components include an ozone generator, oxygen concentrator, venturi mixing device, mixing tank or vessel, ozone concentration monitor, ambient ozone monitor, various valves, and sometimes an ultraviolet (UV) lamp for ozone destruction (see Figures 1 and 2).

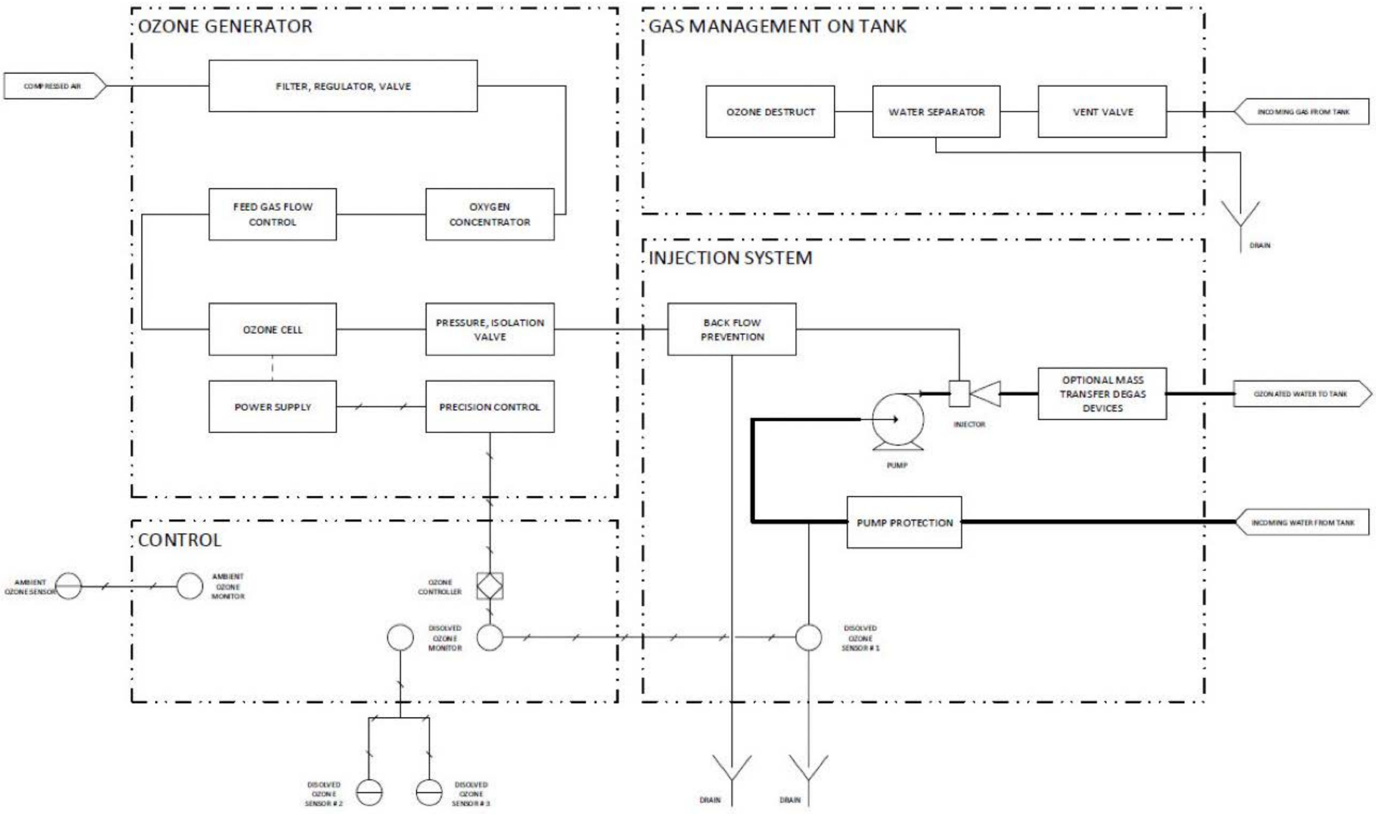


Figure 2: Packaged ozone system process and instrumentation diagram.

Table B: Compensating for Ozone Half-life

03n/HLOC=03c

Where:

03n: Not compensated for half-life of ozone destruction, amount of ozone required to achieve and maintain desired ozone concentration.

HL: Half-life of ozone according to the water temperature from Table A.

03c: Compensated or actual amount of ozone required to be injected in order to maintain residual concentration at the actual water temperature.

Using the relationship and above data, in this case at 25 C, 10 g/0.25 hr=40 g or four times more than without compensation for ozone destruction in water because of half-time.

Source: "How to Compensate for Half-life of Ozone." ©Absolute Ozone

The ozone generator is the system's workhorse, using the corona discharge method to generate ozone from oxygen. The oxygen concentrator uses compressed air, which has an oxygen level of approximately 20% and increases the oxygen level to approximately 90% as feed gas to the corona discharge unit of the ozone generator.

The ozone gas is transferred into the water stream using a venturi or another microbubble device. This dissolves the ozone gas into the water and promotes the mass transfer process. A properly selected venturi, related piping and pump arrangements determine the gas-to-liquid ratio to meet design requirements. A packaged ozone system incorporates an injection assembly that may include a venturi, nozzles, shearing devices, and/or gas separators that define the pump characteristics required for the process.

The ozonated water is delivered to a tank or vessel to oxidize and destroy carbon-based organics in the water. Good mixing and fluid dynamics in the tank are integral and should also be part of the system design. Tank nozzles, connection locations, level, and flow conditions should all be considered. Flow-through characteristics within the vessel and DO3 monitor location ensure uniform mixing, tight control capabilities, and avoid short circuiting.

Precise DO3 concentration control within the tank under all operating conditions is imperative to achieve expected destruction of organics and microbials. [3] DO3 concentration monitors measure ozone concentration in real time in parts per million or parts per billion. Feedback control signals the ozone generator to adjust the gas output to maintain a targeted DO3 concentration and microbial-free system. An ozone gas monitor for the airborne environment is installed for safety (Figure 2). [4]

ADVANTAGES OF PACKAGED OZONE SYSTEMS

Even the best biopharmaceutical water systems are dynamic, with seasonal and other influences that can cause chemistry and temperature changes that affect the growth and concentration of microbials and organic material. Despite fluctuations in the water quality, properly sized packaged ozone systems can maintain pristine conditions using science-based approaches for control, monitoring, and administration. [5] They can be easily controlled to increase or decrease ozone production.

MTE-verified ratios are straightforwardly calculated and ozone demand can be compensated for in real time when fluctuating water chemistry or loading occurs. When devising IOQ and range tests, ozone production can be adjusted and monitored to match intended output and concentration. Packaged ozone systems can be tested under wet conditions and thus commissioned and qualified, verified, validated, and used in PAT schemes. Packaged ozone systems replace uncertain or ill-defined output with a science-based, quantifiable output.

The systems' immediate feedback, control mechanisms, and built-in safety features can alleviate onerous IOQ and validation procedures and adhere to PAT protocols. Since all data is recorded and available while complying with FDA's 21 CFR part 11, current good manufacturing practice compliance is discernible.

Fully automated packaged ozone system

References

1. *Comparison of Ozone and Hot Water Sanitization in Pharmaceutical Water Systems*. Cohen and Nissan, ISPE Water Conference, June 2010, Arlington, VA.
2. *The Efficacy of Ozone and Chemical Sanitization for Microbial Control*. Cohen and Nissan, Ultrapure Water Pharmaceutical Conference. June 2013, Lombard, Ill.
3. *Understanding Dissolved Ozone and Its Use in Pharmaceutical Water Systems*. Cohen and Nissan, Pharmaceutical Engineering Knowledge Brief, KB-0028-MAY13, May 2013.
4. *Limits for Air Contaminants*. US Code of Federal Regulations. Title 29, Standard 1910.1000 Table Z-1.
5. *Ozone Sanitization of Pharmaceutical Water Systems Good Practice Guide*. ISPE, July 2012.

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